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BY

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By E. F. Bashford, M.D.

It would imply an unusual degree of temerity were I, unsolicited, to address, on my present subject, an audience mainly interested in therapeutics. Since, however, you have been so good as to invite me to do so, I presume you appreciate that I do not come before you to talk about the treatment of cancer, except in so far as my remarks are an account of the present position of the attempt to define the direction along which a rational treatment may ultimately be found.

One of the fundamental results of the successful transference of cancer from one animal to another is the attainment of entire agreement as to what it implies. The experimental transference of cancer is effected only by the transplantation and the continued growth of living cancer-cells. Now, although it may be going too far to assert that the disease is never transferred naturally in this way, it is nevertheless certain that the transference of living cells from one individual to another is not the cause of the great frequency of cancer. I do not propose to discuss the ætiology of the disease; nevertheless, in the reactions to which I shall draw your attention you will be presented with some of the evidence proving not only that cancer in one species has no immediate relation to cancer in another species, but also that in different individuals of the same species it arises independently of pre-existing cases. The general conception of the ætiology of the disease underlying my remarks is, cancer arises *de novo* in each individual attacked.

I shall not detail the opposition which has had to be overcome from 1902 onwards in substantiating the claim that cancer in man and animals is a similar biological process, nor shall I worry you with

proofs that all the characteristic lesions of the disease can be reproduced experimentally. The first duty of those engaging in the experimental study of any disease is the reproduction of its characteristic lesions in previously healthy animals. Only thereafter may attempts to demonstrate the prevention or cure of the lesions claim justification, if the disease, as it occurs naturally, remain obdurate to attempts to modify or to end its progress.

Cancer is ubiquitous throughout the vertebrate kingdom, and before alluding to the significance of the reactions revealed by the study of suitability and resistance to the transplantation of cancer, I would direct your attention to the results of the investigation of zoological relationship by methods other than those of the systematic zoologist. The rational experimental investigation of cancer has followed upon the recognition of the importance of the biological differences revealed by the study of the hæmolysin, precipitin, and kindred reactions. By these experimental methods a scale of protein relationships has been ascertained to obtain in the animal kingdom. These reactions are elicited not only by the living cells; they are also functions of the protein substances. By means of these delicate reactions animals as nearly related zoologically as the mouse and the rat are shown to differ widely in the nature of their respective proteins.

Great expectations of a rational organo-pathology and organo-therapy were awakened when these lines of investigation were being explored for the first time, and cytotoxins were produced for special tissues on which they acted in the test-tube. When it was discovered also that the actions could be prevented by the intervention of anti-bodies, optimistic views prevailed as to the possibilities of treating several diseases of obscure ætiology. Cancer was naturally one of the diseases which attracted attention early, because of the hope of obtaining a serum acting upon the cancer-cells. But the wide expectations aroused at the outset of this line of inquiry have not been fulfilled in its later developments, either where they were entertained in regard to the experimental production of disease—e.g., of the nervous system—or where they were entertained in regard to the therapeutics of disease—e.g., in the treatment of cancer. The triumphs of this line of inquiry have lain in the realms of diagnosis and of legal medicine.

In considering the stagnation which has overtaken some aspects of these lines of investigation, it is necessary to note two limitations which ought to have weighed with those responsible for pointing out a vaster vista of progress in cellular pathology and therapeutics than has actually

been visualized: (1) These reactions were obtained by the introduction of tissues of one species into a strange species, and (2) they were demonstrated *in vitro*. It is certainly a startling fact that animals, not only nearly related, but also actually living on the same food, even on the pasture of the same field, build up living protein recognizable zoologically and to the unaided eye—e.g., as horse, cow, goat, sheep, hare, rabbit, and guinea-pig—and as dead protein distinguishable in the test-tube, in consequence of the specific serum reaction the protein substance of any one species elicits when introduced into the body of any other—e.g., when the blood of the hare is introduced into the rabbit, or vice versâ. It is quite easy to beg the questions raised by the fundamental biological fact of proteins so different being built up from the same raw food-stuffs, by rejoining: "Of course, the starting point has not been the food, but the already living protein molecule—Jacques Loeb's autocatalysator—provided by the pre-existent cows or rabbits, &c." Whether the food is broken down into the same elements in the digestive canal of all the above-mentioned herbivora or not, the proteins resulting from the raw food-stuffs are so very different as those of the cow and rabbit, or so similar and still different as those of the mouse and rat. The preceding considerations mark obviously a big advance in knowledge gained since the days when surgeons attempted to graft the skin of rabbits or kittens on to human beings, or transfused the blood of the sheep into human patients. As regards cancer, they show how irrational was the attempt to transfer it from one species to another, except on the assumption of the presence of a cancer parasite of the existence of which experiment has yielded no positive evidence.

In general, the more remote the relationship of the species whose tissues or fluids are employed to elicit these *in vitro* reactions, the more easily are they demonstrated. The animal immunized against strange blood does not produce a hæmolysin acting on the red cells of its own species, and when a hæmolytic immune-serum is not strictly specific—i.e., acts on the blood of more than one species—its action can be simplified, as regards any particular species, by employing that species to yield the hæmolytic immune-serum. Whenever it has been attempted to elicit a corresponding reaction *in vitro* after introducing the blood of one individual into another of the same species, dubious or completely negative results have followed, with the single exception of a series of experiments performed on goats; the feebleness of the reaction (isolysin) demonstrated as compared with that obtainable with strange species (heterolysin) made, at the time when these experiments were

performed, a deep impression upon me which lasts to this day. The attempt to produce experimentally a corresponding reaction *in vitro* by introducing again into an individual some of its own blood (autolysin) has failed altogether, although it has been claimed that the corresponding reaction has been obtained for spermatozoa (auto-spermotoxin).

A corollary to this line of investigation arose in the difficulty of obtaining *in vivo* the cellular reactions apparently so specific *in vitro*. Sera highly cytotoxic for a specific tissue *in vitro* were without action, or, at any rate, any action exhibited was not specific when tested *in vivo* —e.g., auto-spermatoxin and hetero-spermatoxin did not attack the spermatozoa *in vivo*, but only *in vitro*. An exception to this generalization appears to be offered by the action of gastrotoxic serum; but even in this connexion I should be inclined to sound a note of warning. Gastric ulcers appear to have followed only upon the injection of gastrotoxic serum, either intraperitoneally or locally. Although, in regard to the success attending its employment for this specific purpose, gastrotoxic serum appears to stand alone among the heterologous cytotoxic sera, I am unaware of any evidence of the production of a specific gastrotoxin either by homologous or autologous inoculation of gastric mucous membrane. With regard to cancer, the sera obtained from animals of one species after immunization with the tissues of malignant new growths of another species have no reaction *in vitro* distinguishable from the well-known hæmolysin and precipitin reactions. The reactions of an "anti-cancer" serum obtained by immunizing one species with the cancerous tissue of another species are in all respects parallel to those by which blood relationship has been established, and are equally subject to limitations of their action *in vivo*. It may be stated with confidence that all claims to influence the growth of cancer by any such "anti-cancer serum" are based up to date upon fallacies of one kind or another. One thing stands out of all others—viz., the difficulty of demonstrating *in vitro* any reaction with serum obtained after the introduction of homologous or autologous tissue. The search for hæmolysins, cytotoxins, and corresponding reactions[1] demonstrable *in vitro* due to the production of anti-bodies, becomes uncertain when reactions are sought between individuals of the same species, and it becomes altogether hopeless when it is sought to induce reactions between an organism and its own tissues.

It is at this point that the reactions revealed *in vivo* by the experimental study of cancer take up the thread of the progress of experimental

[1] The isoagglutinins are probably an exception.

biology. In contrast to the hæmolytic and kindred reactions obtained by heterologous immunization, the reactions having direct bearing upon cancer are only manifested *in vivo*, and they are elicited not only by immunization with homologous but also with autologous tissue. As I have said, we have good reasons for assuming the autochthonal and *de novo* origin of cancer; wherever it occurs the cancerous tissue may be regarded as part and parcel of the individual attacked. I ask you to consider the reactions of suitability and resistance to the implantation of cancerous tissue into other animals, from the standpoint that the study of the lesions of experimental cancer, and of the means of modifying them, is a necessary preliminary to unravelling the phenomena of spontaneous cancer. As I have often emphasized, the conditions differ in the two cases, because in experimental cancer we observe the behaviour of the tumour-tissue of one animal in a multitude of other animals, whereas in spontaneous cancer the tumour is tissue of the animal attacked.

In the first place I would point out the extreme delicacy and the demonstrative clearness of the reactions revealed by using living cells and living animals as indicators of biological differences, either naturally existing or experimentally induced. Whereas the specific nature of the precipitin reaction revealed unsuspected differences between the body fluids and the tissues of even nearly related species living on the same food, the transplantation of cancer has revealed differences in animals of the same species racially distinct. Further, it has revealed differences in animals of the same race but of different age, and also differences in animals of the same race and age. It has defined still more subtle differences by revealing those obtaining even in animals of the same race and age when naturally afflicted with cancer of the same organ—e.g., the mamma; it has demonstrated that different tumours of a single organ elicit a specific connective tissue and vascular scaffolding, thereby revealing differences between cells histologically indistinguishable. In addition, the transplantation of cancer has made the study of the *vita propria* of the cancer-cell possible. It has revealed, among other facts, the multiplicity of varieties of cancer-cells which may arise from the normal epithelium of a single organ. I must pass over this aspect of the experimental study of cancer, notwithstanding that it possibly contains the germ of a full comprehension of the nature of the disease. I will allude only to a yearning expressed thirty-five years ago: "What a subject for Darwin would be the cells of a cancer if only they were tangible; how the immortal pigeon would be completely eclipsed,

while the hungry pathologist would be filled with food, if only we could observe the variation of tumours under judicious cultivation!" [1] The goal yearned for in this dream of thirty-five years ago, to which Sir Samuel Wilks, being aware of the trend of our work, has drawn my attention, is no longer an unattained ideal, but an accomplished fact to-day. Some seventy distinct varieties of carcinoma descended from normal mammary epithelium, as well as their sub-varieties, are under observation in the Laboratory of the Imperial Cancer Research Fund. Ignoring the wider significance of the experimental study of its *vita propria*, I will summarize the practical importance of the cancer-cell having been made "tangible" by asserting that no method at present available reveals, both for organisms and for living cells, such fine biological differences as those which are so clearly demonstrated by implanting the living cancer-cell into animals, where it can be subjected to many experimentally induced conditions.

The fact is of great biological moment that cancer of one species will not grow continuously in another species; but from the standpoint of immunity, it is to be regarded simply as a consequence of the cancerous tissue being merely the protein of a strange species. Therefore, it is not surprising that animals after preliminary treatment, either with the cancerous or normal tissue of a strange species, are not thereby made resistant to a subsequent inoculation of cancer of their own species. This phenomenon is demonstrated in the accompanying figures,[2] where rats previously "treated" with sarcoma of the cat and mouse respectively are shown to remain suitable for the inoculation and growth of rat sarcoma or carcinoma. Similar negative results, as regards immunity, obtain if animals are first treated with normal tissues of strange species. The accompanying figures show how rat skin employed in this way is impotent to protect mice against the implantation of squamous-celled carcinoma of the mouse. Other figures illustrate the nature of the change ensuing after a preliminary inoculation of normal or of tumour tissue of a strange species, as it is revealed by examination of the site where subsequent re-inoculation is made. The reaction elicited by the preliminary inoculation is reinforced at the re-inoculation, and, in addition, influences directly lethal to the introduced tissue are obviously in play. This is only a consequence one would expect from a procedure

[1] James F. Goodhart, M.D.: "On Cancer as illustrated in Ichthyosis of the Tongue and Allied Diseases resulting from Prolonged Local Irritation," *Guy's Hosp. Reports*, 3rd Ser., 1875, xx.

[2] The paper was illustrated by a number of lantern slides, but corresponding figures do not accompany its publication in the *Proceedings* of the Section.

which is parallel with that employed to obtain heterologous immune-sera having a cytotoxic action *in vitro;* but it is far from being an immunity reaction to cancer *qua* cancer.

Cancer tissue will only grow continuously in other animals of the same species as that in which the tumour developed, where alone the necessary food-stuffs are supplied. The question of pabulum is, however, not the only matter of moment, as the following considerations show. When a malignant new growth is removed from the individual mouse in which it developed, and implanted into a number of healthy mice, rarely do the implantations take in more than 12 per cent., and the results may be entirely negative in as many as 900 attempts. It has been customary to explain the negative results of this homologous transplantation by assuming that the majority of healthy animals are naturally resistant to the inoculation of cancer of their own species. But as an interpretation of the facts the term "natural resistance" is nothing more than a meaningless phrase. In addition to the two variables which were at once recognized—viz., the varying qualities of the animals and the varying qualities of the tumour cells—quite a number of others have already been defined. Such investigations, however, bear more on the nature of cancer than on the induction of immunity, and I pass them over after merely intimating that, although it is difficult, and sometimes impossible, to obtain the continued growth of a tumour in normal animals, recent extensive re-investigations of the results of transplanting tumours back again into the animals in which they developed have greatly improved upon the results previously recorded. They have demonstrated that auto-transplantations are successful, under given conditions, in 95 per cent., and thereby the frequency of large metastases in animals spontaneously affected is harmonized with the difficulties in obtaining growth by implanting the tumour of an animal naturally affected into normal animals, or into other animals naturally affected with cancer. The next series of considerations have some bearing upon why transplantation into other animals of the same species (homologous transplantation) so frequently fails.

Reactions inimical to the implantation and the continued growth of cancer-cells are induced in living animals by preliminary treatment with homologous tissue, either cancerous or normal. The figures illustrate how high a degree of resistance may result to subsequent inoculation after tissue has been absorbed in this way. More interesting still is the fact that this form of resistance may be induced concomitantly with the establishment of a tumour, and indeed may be so effectively induced as

to cause, on the one hand, a large proportion, or even all the tumours developing, to exhibit only transitory and not progressive growth, or, on the other hand, to render the animals resistant to a secondary inoculation, when the tumours from the first inoculation continue to grow. This resistance presents many interesting features. In the first place it is specific; the resistance induced by the absorption of tumour tissue is most effective against a re-inoculation of the tumour absorbed, and may be almost ineffective against other tumours. Thus, a complete resistance to the implantation of a carcinoma is compatible with a suitability for the implantation of sarcoma. The preliminary absorption of different normal tissues is of varied efficacy. One may say skin protects best against the inoculation of skin cancer; but skin also protects best against the inoculation of mammary carcinoma, and the apparent relation between the protection induced by normal tissue as against tumours of the corresponding histological structure cannot be referred only to similarity of histogenesis without important reservations. The perfect protection mouse skin induces against squamous-celled carcinoma of the mouse, and the absence of this action in the case of skin of the rat, is very striking; but the efficacy of mouse skin as a protector depends—apart from the main factor that it is mouse tissue—also on such technical factors as those of dosage, which obscure, if they do not outweigh, the importance of the histological relationship of the skin of the mouse to squamous-celled carcinoma of the mouse. The spleen also induces a high degree of protection against epithelial tumours. The analysis of the induction of artificial resistance can be carried still further. The subcutaneous inoculation of tissue removed from an animal and immediately re-inoculated into itself effectively induces protection, as illustrated, for the autologous inoculation of spleen.

It has thus been shown that there is a parallel in the behaviour of cancerous tissue and of normal tissue of the same species, in regard to their powers of inducing protection against inoculation; and, further, it has been shown that it is immaterial whether the normal tissue is provided by another animal (homologous inoculation) or by the very animal itself (autologous inoculation). The ease with which these reactions are obtained *in vivo* and their demonstrative clearness are in marked contrast with the difficulty of obtaining "isolysin" reactions *in vitro* and the failure to obtain any corresponding "autolysin" reaction at all, either *in vitro* or *in vivo*. The mechanism of resistance after immunizing with homologous normal or tumour tissue is also in marked contrast to that described above as obtaining in the case

of the heterologous reactions *in vivo* after preliminary treatment with cancer or normal tissue of strange species. It has been impossible to obtain any effect *in vitro* of the serum of animals immunized with homologous tissue or tumour which is not possessed in equal degree by normal serum. All attempts to detect anti-bodies transferable from one individual to another, or from the pregnant or suckling mother to her offspring, have failed. The quantitative relations obtaining between the degree of immunity and the dose of material which induced it, as well as between the degree of immunity and the doses of tumour against which it is effective, speak for the intervention of active substances or forces of some kind which can be used up. There is also some evidence of direct interactions taking place in the body fluids of immunized animals so that the degree of immunity can be lowered. Although it is difficult to conceive that alterations in the body fluids are not in part responsible for the change, there is no evidence of a direct lethal action on the cancer-cells, which remain alive the longer the nearer they are to the tissues and fluids of the immune animal, exactly the opposite being the case for heterologous inoculations, as described above. The change manifests itself, during the process of immunization, by a general reaction (plasma-cell reaction) of the entire connective tissue of the animal. When immunity is established, it manifests itself in a paralysis of the chemiotactic powers of the cancer-cells; when implanted into an immune animal, they fail to elicit the connective tissue and vascular scaffolding necessary for their growth into a tumour. The result is the contrast between the appearances at the site of inoculation in a normal and in an immune animal, as depicted in the accompanying figures.

For the further elucidation of the process extensive studies have been necessary on the consequences following the inoculation of the protein substances both of normal and of cancer-cells, as distinct from the inoculation of the living cells themselves. In this respect, also, there is an entire parallel between the behaviour of the proteins obtained from normal and cancerous tissue. They do not induce immunity, and thereby yet another distinction is established between the hæmolytic, precipitin and kindred reactions, elicited by heterologous inoculation and demonstrable *in vitro;* because the latter are independent of the vital integrity of the tissue inoculated. In this connexion it may be permitted to draw attention also to the difference between the immunity reactions to many bacteria and their products. Leaving out of consideration those cases in which soluble toxins can be separated from the organisms, the latter reactions, with some exceptions, are not usually

or even generally regarded as dependent upon the inoculation of living organisms. It might appear that the loss of power to elicit immunity to cancer by the inoculation of homologous or autologous protein, as distinct from living cells, was merely the consequence of the indifferent nature of the proteins when re-inoculated into animals of the same species, or even into the same individual. That this is not the explanation is proved by the fact that the proteins when so inoculated are not indifferent, but may actively modify the animals in the direction of rendering them more suitable for inoculation. Here I am tempted to make a digression into bacteriology and to ask the question: Does the inoculation of bacteria, *killed* by heat or otherwise, always have consequences only milder but otherwise identical with the inoculation of living bacteria? I am aware it is generally assumed that there is only a quantitative, and not a qualitative, difference in the reactions to living or dead bacteria which are the specific cause of well-defined diseases, but the marked qualitative differences in the effects following the inoculation of the living and the disintegrated cancer-cell give cause for thought. I express no opinion on this matter beyond recommending it to the consideration of others more competent than myself to deal with it. But I do hold very strong opinions on another matter—namely, on the indiscriminate practice of what, with reference to cancer, is erroneously styled vaccine-therapy. Some of these procedures practised with organisms, perhaps carelessly killed, may, in unskilful hands, have consequences exactly the reverse from those anticipated, having regard to the fact that hypersensitiveness, and not immunity to the inoculation of cancer, can be induced by heterologous tissue and other agents. It has been experimentally demonstrated that as yet no outlook is opened on the therapeutics of cancer by employing killed cancer-cells, tumour extracts, or vaccines of supposititious cancer parasites. The employment of such empirical means as vaccines of *Bacillus neoformans*, of various cocci, of antiyeast, and other heterologous antisera as curative agents for malignant new growths has no scientific justification whatsoever. These methods of treatment are merely modern forms of empiricism. The claim has been made that the employment of the mixed toxins of streptococci and *Bacillus prodigiosus* is justified on experimental grounds. The experiments relied upon were performed on dogs affected with growths having a histological structure like that of lympho-sarcoma. These growths are, however, infective venereal tumours, and fundamentally different both in their clinical history and their pathology from the sarcomata and carcinomata, whether occurring in dogs or in man.

Throughout the sequence of observations recorded above on the parallel behaviour of normal and cancerous tissue you will have noted that the tumour tissue used, whether for preliminary treatment in order to immunize, or for testing the animals after treatment, has usually been derived from another animal. You will have noticed also that I have referred only to the effects obtained in normal animals, and not to any effects obtained in animals already bearing tumours. This is because our observations are advancing only slowly from one sure step to another. As yet they have yielded unequivocal results only under the experimental conditions above described. It is, however, obvious that if cancer arises *de novo* in the individual attacked, then the problem of immunity to cancer, as defined by the experiments already described, resolves itself into the problem of immunizing an animal against its own tumour tissue, and, further, involves the problems of modifying both the growth of tumours already existing and of immunizing animals against the dissemination of tumours when present. The interpretation of immunity to the implantation of cancer as a "vaccination" against the natural onset of the disease, involves a grave misunderstanding of the significance of the observations. I have often emphasized the necessity for awaiting the application of modern experimental methods to animals bearing spontaneous tumours, before drawing any deductions as to the bearing of the results on the cure or prevention of cancer occurring naturally. Some years ago I re-enforced this warning by pointing out that mice which are effectively protected against the implantation of cancer may develop tumours of their own spontaneously. The need for caution must be pointed out still more emphatically to-day, since as the number of investigators who have observed immunity to implanted cancer increases, so also does the number of voices proclaiming the possibility of "vaccinating" human beings against cancer increase. I would not impress you as being pessimistic, but I would remind you of the years that have usually elapsed before the methods successful in controlling or curing diseases induced experimentally in animals, have developed into methods which could be successfully applied to man. The systematic experimental study of cancer is of scarce seven years' duration. The definite results foreshadowing others of possible therapeutical bearing have been obtained only in the case of *normal animals* made to bear transplanted tumours obtained from *other animals*. It is possible to prevent any implantation from taking in a normal animal, but a conundrum not yet satisfactorily solved is, why the means which succeed so well in normal animals are very much less certain,

and, under given conditions, usually fail to prevent an implantation into an animal already bearing a transplanted tumour. These investigations have, of course, important bearings upon the continued growth of a tumour once it is present, and possibly even more direct bearings upon dissemination. Our attacks on this problem now extend over the four years which have elapsed since experiment disclosed that it existed. Persistent endeavour is being met with gradually improving results: the growth of an established tumour can be somewhat modified by the inoculation and absorption of tumour tissue, and secondary inoculations in animals already bearing tumours can be prevented by the presence of an active resistance which has been induced in a similar way. The questions here are not only those pertaining to the influence a growing tumour may exercise upon its host, but are also those of mastering important matters of technique, and of hunting for and utilizing that material which affords opportunity for arranging the suitable experimental conditions. I do not propose to go beyond stating there is ground for hopes that the difficulties will be overcome as many others have been. There is encouragement in the indications that the growth of established tumours can be experimentally retarded as well as in the evidence that secondary implantations (artificial metastases) can be prevented in tumour-bearing animals. In both respects the indications are as suggestive and encouraging as those which five or six years ago presaged the now undisputed achievement that the implantation of cancer can be prevented with absolute certainty. At present no such definite conclusion can be drawn as to the prevention of natural metastases. The control of transplanted tumours and of the elaboration of methods of immunizing a tumour-bearing animal against a secondary inoculation (artificial metastases) will probably precede the formulation of what the immunity reaction to cancer precisely involves. This being so, it will be premature to enter into any lengthy discussion of our experiments on animals naturally affected with cancer. The large number of such tumour-bearing animals at our disposal has already made many preliminary observations possible, but till the above problems are solved we are working more or less in the dark, and it may be along entirely erroneous paths. The frequency with which the cure of transplanted tumours takes place as contrasted with the rarity of the occurrence in mice spontaneously attacked presents a problem the meaning of which is only dawning upon us. Out of some 400 mice affected with spontaneous cancer, the clinical course of which has been followed with the greatest care for weeks or months, we have observed

unequivocal evidence of natural healing—circumscribed or complete—only some three or four times, whereas transplanted tumours may disappear in any proportion up to 100 per cent., according to the nature of the tumour and the technique employed. However, natural healing of spontaneous tumours does occur both of the primary growths and of the metastases. Its rarity is no evidence against an immunity reaction to cancer existing—it certainly does exist—but its final elucidation will probably be ascertained by studying the reactions occurring within the body of an animal bearing a tumour which is part and parcel of its own body. Experiment has already given us the clues I have mentioned, and I hold it is not a vain dream to anticipate the experimental discovery of others as yet unsuspected.

I have illustrated how the problems of the immunity reaction to cancer are being narrowed down; to recall only one instance, I showed you that the absorption of an animal's own tissues can modify the animal so fundamentally as to render it absolutely resistant to the implantation of cancer. Were this the only new fact ascertained it would of itself introduce fresh conceptions into pathology and biology. I need not allude to the far-reaching importance of the many entirely new facts that have been revealed by the study of homologous and autologous inoculations; they have opened up an entirely new chapter in the biological analysis of the living organism. We shall learn more of them in further attempts to define the immunity reaction to cancer, and, if years elapse before this goal is attained, I venture to believe that the experimental study of cancer will, in the interval, have made a lasting impression upon pathology and a still greater one upon general biology.

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